08/27/04 IFW

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 04-101-C)

In the Application of:	)	
	)	
Bucciarelli et al.	)	
	)	**Examiner:**
Serial No.: 10/646,129	)	
	)	**Group Art Unit: 1644**
Filing Date: August 22, 2003	)	
	)	
For: Methods and compositions for increasing Protein yield from a cell culture	)	

TRANSMITTAL LETTER

Commissioner for Patents
Alexandria, VA 22313-1450

Dear Sir:

In regard to the above identified application,

1. We are transmitting herewith the attached:
   a) Information Disclosure Statement;
   b) PTO Form 1449 and cited references;
   c) Return postcard

2. With respect to fees:
   a) No fees are required
   b) Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.

3. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage Express Mail in an envelope addressed to the Commissioner for Patents, Alexandria, VA 22313-1450 on August 26, 2004.

Respectfully submitted,

Date: August 26, 2004

Kevin E. Noonan, Ph.D.
Registration No. 35,303

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, IL 60606
(312)913-0001

PATENT
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 04-101-C)

In the Application of:	)	
	)	
Bucciarelli et al.	)	
	)	**Examiner:**
Serial No.: 10/646,129	)	
	)	**Group Art Unit: 1644**
Filing Date: August 22, 2003	)	
	)	
For: Methods and compositions for increasing Protein yield from a cell culture	)	

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. Copies of the references cited below are enclosed. These references are also listed on the enclosed PTO Form 1449.

In the judgment of the undersigned, portions of the listed references may be material to the Examiner's consideration of the presently pending claims. This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

Applicants do not believe any fee is due with this submission. If this belief be in error and the Patent Office determines that the fee prescribed in the relevant portion of 37 C.F.R. Section 1.97 is applicable, the undersigned representative by his signature hereby authorizes any such fee to be debited from Deposit Account 13-2490.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Date: August 26, 2004

Kevin E. Noonan
Reg. No. 35,303

Substitute for form 1449A/PTO				Complete if Known	
				Application No.	10/646,129
				Filing Date:	8/22/2003
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				First Named Inventor	Bucciarelli et al.
				Group Art Unit	1644
(use as many sheets as necessary)				Examiner Name	
Sheet	1	of	6	Attorney Docket No.	04-101-C

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Document Number	U.S. Patent Document Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Figures Appear
	1	6,274,341	B1	Bailey et al.	08-14-2001	
	2	5,891,718		Hobart et al.	04-06-1999	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office[3]	Foreign Patent Document Number[4]	Foreign Patent Document Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Figures Appear	T[6]
	3	WO	94/04672	A1	DNZ Corp.	03-03-1994		

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [6] Applicant is to place a check mark here if English translation is attached.

Substitute for form 1449A/PTO				Complete if Known	
				Application No.	10/646,129
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Filing Date:	8/22/2003
				First Named Inventor	Bucciarelli et al.
				Group Art Unit	1644
(use as many sheets as necessary)				Examiner Name	
Sheet	2	of	6	Attorney Docket No.	04-101-C

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.[1]	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	4	Campisi *et al.*, "Cancer, Aging and Cellular Senescence" *in vivo* 14:183-188 (2000).	
	5	Serrano *et al.*, "A new regulatory motif in cell-cycle control causing specific inhibition of cyclin D/CDK4" *Nature* 366:704-707 (December 16, 1993).	
	6	Rivard *et al.*, "Abrogation of p27Kip1 by cDNA Antisense Suppresses Quiescence (Go State) in Fibroblasts" *The Journal of Biol. Chem.* 271(31)18337-18341 (1996).	
	7	Kato *et al.*, "Cyclic AMP-Induced G1 Phase Arrest Mediated by an Inhibitor ($p27^{Kip1}$) *Cell* 79:487-496 (November 4, 1994).	
	8	Weber *et al.*, "AnSV40 "Enhancer Trap" Incorporates Exogenous Enhancers or Generates Enhancers from its Own Sequences" *Cell* 36:983-992 (April 1984).	
	9	Lukas et al., "Retinoblastoma-protein-dependent cell-cycle inhibition by the tumour suppressor p16" Nature 375:503-506 (June 8, 1995).	
	10	Ewen et al., "Functional Interactions of the Retinoblastoma Protein with Mammalian D-type Cyclins" Cell 73:487-497 (May 7, 1993).	
	11	Coats et al., "Requirement of $p27^{Kip1}$ for Restriction Point Control of the Fibroblast Cell Cycle" Science 272:877-880 (May 10, 1996).	
	12	Xiong et al., "p21 is a universal inhibitor of cyclin kinase" Nature 366:701-704 (December 16, 1993).	
	13	Resnitzky et al., "Acceleration of the G_1/S Phase Transition by Expression of Cyclins D1 and E with an Inducible System" Molecular and Cellular Biology 1669-1679 (March 1994).	
	14	Matsuoka et al., p57KIP2, a structurally distinct member of the p21CIP1 Cdk inhibitor family, is a candidate tumor suppressor gene" *Genes & Development* 9:650-662 (1995).	
	15	Cristofalo et al., "Enzyme Activity during the Growth and Aging Human Cells in Vitro" Journal of Cellular Physiology 69:263-272.	
	16	Goldstein et al., "Studies on the Molecular-Genetic Basis of Replicative Senescence in Werner Syndrome and Normal Fibroblasts" Experimental Gerontology 24:461-468 (1989).	
Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] Applicant is to place a check mark here if English translation is attached.

Substitute for form 1449A/PTO				Complete if Known	
				Application No.	10/646,129
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Filing Date:	8/22/2003
				First Named Inventor	Bucciarelli et al.
				Group Art Unit	1644
(use as many sheets as necessary)				Examiner Name	
Sheet	3	of	6	Attorney Docket No.	04-101-C

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. [1]	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	17	Polyak et al., "Cloning of $p27^{Kip1}$, a Cyclin-Dependent Kinase Inhibitor and a Potential Mediator of Extracellular Antimitogenic Signals" Cell 78:59-66 (July 15, 1994).	
	18	Levenson et al., "Internal Ribosomal Entry Site-Containing Retroviral Vectors with Green Fluorescent Protein and Drug Resistance Markers" Human Gene Therapy 9:1233-1236 (May 20, 1998).	
	19	Brenner et al. "Increased p16 expression with first senescence arrest in human mammary epithelial cells and extended growth capacity with p16 inactivation" Oncogene 17:199-205 (1998).	
	20	Chang et al., "Role of p53 and $p21^{waf1/cip1}$ in senescence-like terminal proliferation arrest induced in human tumor cells by chemotherapeutic drugs" Oncogene 18:4808-4818 (1999).	
	21	Fabbrizio et al., "Inhibition of mammalian cell proliferation by genetically selected peptide aptamers that functionally antagonize E2F activity" Oncogene 18:4357-4363 (1999).	
	22	Fang et al., "$p21^{Waf1/Cip1/Sdi1}$ induces permanent growth arrest with markers of replicative senescence in human tumor cells lacking functional p53" Oncogene 18:2789-2797 (1999).	
	23	Dimri et al., "A biomarker that identifies senescent human cells in culture and in aging skin in vivo" Proc. Natl. Acad. Sci. 92:9363-9367 (September 1995).	
	24	Chang et al., "Effects of $p21^{Waf1/Cip1/Sdi1}$ on cellular gene expression: Implications for carcinogenesis, senescence, and age-related diseases" PNAS 97:4291-4296 (April 11, 2000).	
	25	Burns et al., "Vesicular stomatitis virus g glycoprotein pseudotyped retroviral vectors: Concentration to very high titer and efficient gene transfer into mammalian an nonmammalian cells" Prod. Natl. Acad. Sci. 90:8033-8037 (September 1993).	
	26	Pear et al., "Production of high-titer helper-free retroviruses by transient transfection" Proc. Natl. Acad. Sci. 90:8392-8396 (September 1993).	
	27	Gray et al., "Exploiting Chemical Libraries, Structure, and Genomics in the Search for Kinase Inhibitors" Science 533-538 (July 24, 1998).	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] Applicant is to place a check mark here if English translation is attached.

Substitute for form 1449A/PTO				Complete if Known	
				Application No.	10/646,129
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Filing Date:	8/22/2003
				First Named Inventor	Bucciarelli et al.
				Group Art Unit	1644
(use as many sheets as necessary)				Examiner Name	
Sheet	4	of	6	Attorney Docket No.	04-101-C

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.[1]	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	28	Schultz et al., "Paullones, a Series of Cyclin-Dependent Kinase Inhibitors: Synthesis, Evaluation of CDK1/Cyclin B Inhibition, and in Vitro Antitumor Activity" J. Med. Chem. 42:2909-2919 (1999).	
	29	Chen et al., "Cyclin-Binding Motifs Are Essential for the Function of $p21^{CIP1}$" Molecular and Cellular Biology 16(9)4673-4682 (Sept. 1996).	
	30	Dimri et al., "Regulation of a Senescence Checkpoint Response by the E2F1 Transcription Factor and p14ARF Tumor Suppressor" Molecular and Cellular Biology 20(1)273-285 (January 2000).	
	31	Hirai et al., "Novel INK4 Proteins, p19 and p18, Are Specific Inhibitors of the Cyclin D-Dependent Kinases CDK4 and CDK6" Molecular and Cellular Biology 15(5)2672-2681 (May 1995).	
	32	Saha et al., "$p21^{CIP1}$ and Cdc25A: Competition between an Inhibitor and an Activator of Cyclin-Dependent Kinases" Molecular and Cellular Biology 17(8)4338-4345 (August 1997).	
	33	Stein et al., "Differential Roles for Cyclin-Dependent Kinase Inhibitors p21 and p16 in the Mechanisms of Senescence and Differentiation in Human Fibroblasts" Molecular and Cellular Biology 19(3)2109-2117 (March 1999).	
	34	Fero et al., "A Syndrome of Multiorgan Hyperplasia with Features of Gigantism, Tumorigenesis, and Female Sterility in $p27^{KIP1}$-Deficient Mice" Cell 85:733-744 (May 31, 1996).	
	35	Schnier et al., "The Kinase Inhibitor Staurosporine Induces G_1 Arrest at Two Points: Effect on retinoblastoma Protein Phosphorylation and Cyclin-dependent Kinase 2 in Normal and Transformed Cells" Cancer Research 54:5959-5963 (November 15, 1994).	
	36	Chang et al., "A Senescence-like Phenotype Distinguishes Tumor Cells That Undergo Terminal Proliferation Arrest after Exposure to Anticancer Agents" Cancer Research 59:3761-3767 (August 1, 1999).	
	37	Akiyama et al., "G_1 Phase Accumulation Induced by UCN-01 is Associated with Dephosphorylation of Rb and CDK2 Proteins as well as Induction of CDK Inhibitor p21/Cip1/WAF1/Sdi1 in p53-mutated Human Epidermoid Carcinoma A431 cells" Cancer Research 57:1495-1501 (April 15, 1997).	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] Applicant is to place a check mark here if English translation is attached.

Substitute for form 1449A/PTO				Complete if Known	
				Application No.	10/646,129
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Filing Date:	8/22/2003
				First Named Inventor	Bucciarelli et al.
				Group Art Unit	1644
(use as many sheets as necessary)				Examiner Name	
Sheet	5	of	6	Attorney Docket No.	04-101-C

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.[1]	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	38	Serrano et al., "Role of the INK4a Locus in Tumor Suppression and Cell Mortality" Cell 85:27-37 (April 5, 1996).	
	39	EMI et al., "Pseudotype Formation of Murine Leukemia Virus with the G Protein of Vesicular Stomatitis Virus" Journal of Virology 1202-1207 (March 1991).	
	40	Toyoshima et al., "p27, a Novel Inhibitor of G1 Cyclin-Cdk Protein Kinase Activity, Is Related to p21" Cell 78:67-74 (July 15, 1994).	
	41	El-Diery et al., "WAF1, a Potential Mediator of p53 Tumor Suppression" Cell 75:817-825 (November 19, 1993).	
	42	Harper et al., "The p21 Cdk-Interacting Protein Cip1 Is a Potent Inhibitor of G1 Cyclin-Dependent Kinases" Cell 75:805-816 (November 19, 1993).	
	43	Driscoll et al., "Cyclin D_1 antisense RNA destabilizies pRb and retards lung cancer cell growth"	
	44	Buchkovich et al., "The Retinoblastoma Protein is Phosphorylated during Specific Phases of the Cell Cycle" Cell 58:1097-1105 (September 22, 1989).	
	45	Deng et al., "Mice Lacking $p21^{CIP1/WAF1}$ Undergo Normal Development, but Are Defective in G1 Checkpoint Control" Cell 82:675-684 (August 25, 1995).	
	46	Koff et al., "Formation and Activation of a Cyclin E-cdk2 Complex During the G_1 Phase of the Human Cell Cycle" Science 257:1689-1694 (September 18, 1992).	
	47	Mazur et al., "Higher Productivity of Growth-Arrested Chinese Hamster Ovary Cells Expression the Cyclin-Dependent Kinase Inhibitor p27" Biotechnol. Prog. 14:705-713 (1998).	
	48	Sherr et al., "Inhibitors of mammalian G_1 cyclin-dependent kinases" Genes & Development 9:1149-1163 (1995).	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] Applicant is to place a check mark here if English translation is attached.

Substitute for form 1449A/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application No.**	**10/646,129**
				Filing Date:	**8/22/2003**
				First Named Inventor	**Bucciarelli et al.**
				Group Art Unit	1644
(use as many sheets as necessary)				Examiner Name	
Sheet	6	of	6	Attorney Docket No.	04-101-C

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.[1]	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
	49	Fussenegger et al., "Genetic optimization of recombinant glycoprotein production by mammalian cells" Tibtech 17:35-42 (January 1999).	
	50	Mazur et al., "A Novel Autoregulated Proliferation-Controlled Production Process Using Recombinant CHO Cells" Biotechnology and Bioengineering 65:144-150 (October 20, 1999).	
	51	Geserick et al., "Enhanced Productivity During Controlled proliferation of BHK Cells in Continuously Perfused Bioreactors" Biotechnology and Bioengineering 69:268-274 (August 5, 2000).	
	52	Taniguchi et al., "Induction of the $p16^{INK4a}$ senescence gene as a new therapeutic strategy for the treatment of rheumatoid arthritis" Nature Medice 5(7):760-766 (July 1999).	
	53	Uhrbom et al., "Induction of senescence in human malignant glioma cells by $p16^{INK4a}$" Oncogene 15:505-514 (1997).	
	54	Carlson et al., "Flavopiridol Induces G_1 Arrest with Inhibition of Cyclin-dependent Kinase (CDK)2 and CDK4 in Human Breast Carcinoma Cells" Cancer Research 56:2973-78 (July 1, 1996).	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] Applicant is to place a check mark here if English translation is attached.